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SHORT COMMUNICATION

Comments on "Gene and genon concept" by K. Scherrer and J. Jost

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I highly appreciate this seminal paper (Scherrer and Jost 2007) which not only provides an overview of the current knowledge of gene expression, but is particularly valuable, as it sets a framework to mathematically assess the information content of hereditary material by separating the capacity to form biologically meaningful polypeptides or structural RNAs (redefined by the authors as "genes") from the ability to comprehensively regulate their formation (defined as "genon"). This choice of the physical entities encompassing the two information carriers constitutes on one hand a convincing novel idea; on the other hand it constitutes the result of the discovery that RNAs are synthesized as long precursors, the definition of multiple steps involved in the regulation of the formation of polypeptides and structural RNAs as end products (cascade of regulation) and the insights in the three dimensional organization of DNA, chromatin and matrix in the nucleus (unified matrix hypothesis).

In my opinion, most of the claims regarding biochemistry, organization of biological structures in 3D space at cellular level and information processing made in the paper are justified. It is remarkable that only few investigators reported such insights, long before they were accepted by the scientific community. Modern disciplines including systems biology, genomics and other—omics are confirming with enormous technical apparatus many of the claims made on the basis of thoughtful experiments, which often raised opposition or ridicule by colleagues sticking in detail and/or simply following widely accepted beliefs.

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Since I am lacking the mathematical background required I am not able to comment on the information theoretic part of the paper. It seems to me that still a lot of work is required to further develop the mathematical tools, which at present appear somewhat oversimplified to the layman. In particular, almost exclusively the coding capacity is addressed mathematically, whereas so far little attention is devoted to the regulatory aspects. It would be most welcome for people with a background only in biochemistry and molecular genetics to provide in the further development of the ideas outlined in the paper also simple examples demonstrating how actual calculations can be carried out.

In their long already published commentary entitled "Genes", Prohaska and Stadler seriously question the merits of the the Scherrrer and Jost paper, pointing out that many downstream regulatory aspects are lacking, including modification of the polypeptides produced, their assembly into functional entities, multiple crosstalk between genes and gene products; one might add that also breakdown of gene products can be regulated. However, recognizing that these aspects are vital for the understanding of living organisms, and that they might never be amenable to quantitative mathematical treatment, I nevertheless think that merely addressing the information inherent in the the primary gene products and in their regulated expression is worthwhile.

Since in my view the life sciences could greatly profit from the further development of the concepts addressed in the Scherrer–Jost paper, it would be vital that the scientific community active in this vast field would accept not only the views expressed, but also the nomenclature introduced. For entirely different reasons the usefulness of both terms "gene" and "genon" appear inadequate for broad acceptance. As the authors point out, the meaning of "gene" is

extensively blurred in the present use; thus it seems hardly possible to narrow down its meaning to that proposed by the authors which, by the way, does not exactly correspond to its original meaning. A new term should thus be coined instead of "gene" referring to the precise proposed structural/functional meaning. As to "genon", this word can be very easily be misunderstood phonetically as "genome" (even in writing "genon" is likely to be confused with "genome", as recently happened in "encounters" published by EMBO). The less confusing term "genopon" would appear more appropriate, as it would additionally render more clearly its assembly from "gene" and "operon", as explained by the authors.

One clarification would also be helpful. While there is no doubt about the primordial significance of full domain transcripts, it should be clearly stated whether in the view of the authors all mRNAs are derived from those exceedingly long transcripts. It does not unambiguously emerge from reading the paper whether under natural conditions the old concept of transcription initiations near TATA boxes should be completely abandoned.

The views expressed above cannot properly address the merits of the paper. In summary, it must be emphasized that the further development of the thoughts outlined by the authors in a more comprehensive book would be highly advisable. Broad acceptance by the scientific community would be of great importance to gain a more comprehensive general understanding of life.

Reference

Scherrer K, Jost J (2007) Gene and genon concept: coding versus regulation. A conceptual and information-theoretic analysis of genetic storage and expression in the light of modern molecular biology. Theory Biosci 126:65–113